A Dissertation on

STUDY ON CLINICAL,SEROLOGICAL, CYTOLOGICAL CORRELATION IN CASES OF AUTOIMMUNE THYROIDITIS.

Submitted to

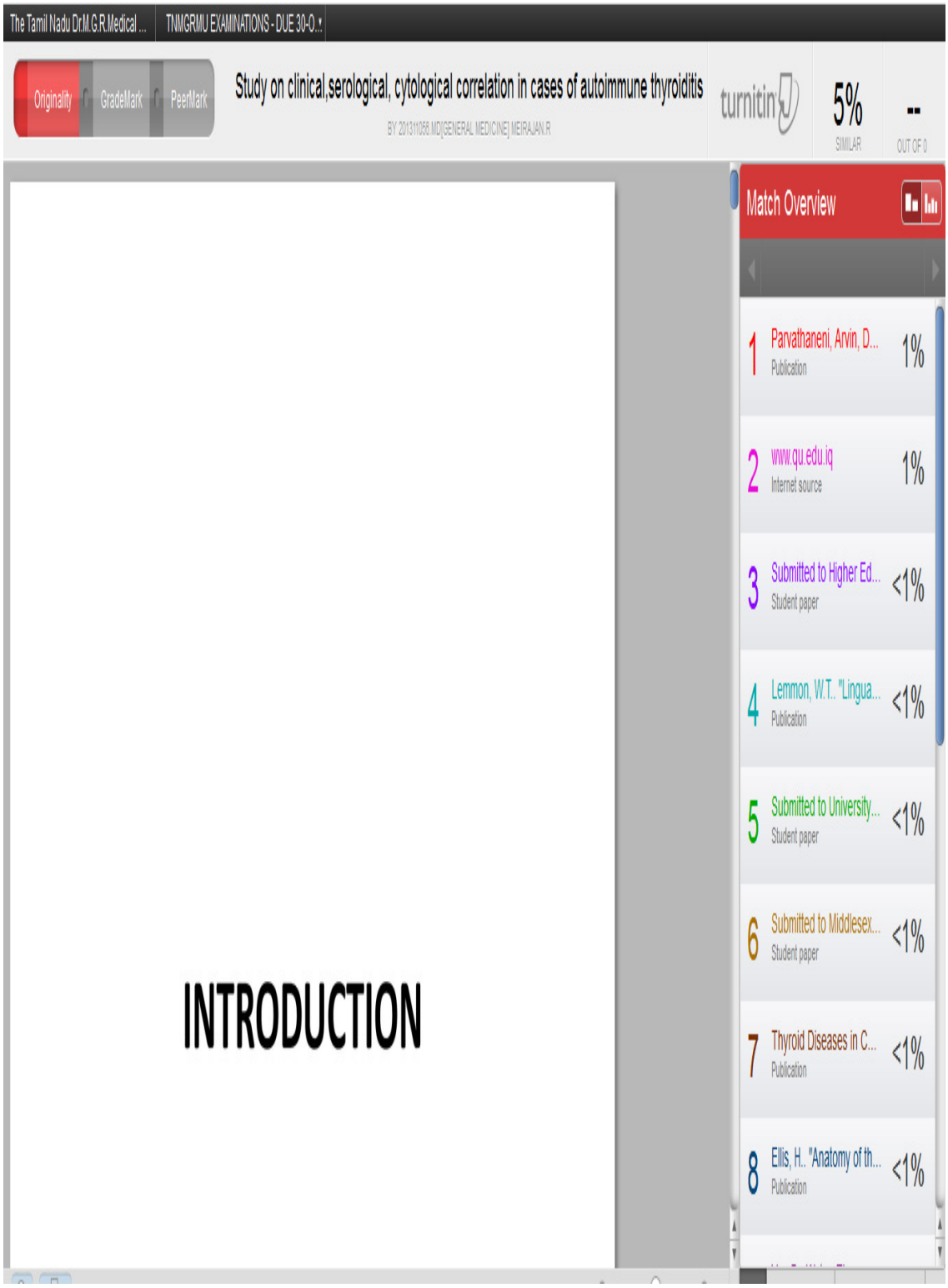
THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600032

In partial fulfilment of the Regulations
for the Award of the Degree of

M.D. BRANCH - I

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE
STANLEY MEDICAL COLLEGE
CHENNAI – 600 001
APRIL 2016


The Tamil Nadu Dr.M.G.R.Medical ...
TNMGRMU EXAMINATIONS - DUE 30-0...
Originality
GradeMark
PeerMark
Study on clinical,serological, cytological correlation in cases of autoimmune thyroiditis
BY 201311068.MD(GENERAL MEDICINE) MEIRAJAN.R
turnitin
5%
SIMILAR
--
OUT OF 0
INTRODUCTION
Match Overview
1 Parvathaneni, Arvin, D... 1%
Publication
2 www.qu.edu.iq 1%
Internet source
3 Submitted to Higher Ed... <1%
Student paper
4 Lemmon, W.T.. "Lingua... <1%
Publication
5 Submitted to University... <1%
Student paper
6 Submitted to Middlesex... <1%
Student paper
7 Thyroid Diseases in C... <1%
Publication
8 Ellis, H.. "Anatomy of th... <1%
Publication

CERTIFICATE BY INSTITUTION

This is to certify that **DR.R.MEIRAJAN,** Post - Graduate Student (JULY 2013 TO APRIL 2016) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600 001, has done this dissertation on "**STUDY ON CLINICAL,SEROLOGICAL, CYTOLOGICAL CORRELATION IN CASES OF AUTOIMMUNE THYROIDITIS"** under my guidance and supervision in partial fulfilment of the regulations laid down by the TamilNadu Dr.M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2016.

Dr.R.JAYANTHI M.D

Professor & HOD

Department of Medicine

Govt. Stanley Medical

College & Hospital

DR.ISAAC CHRISTIAN MOSES

M.D,FICP,FACP

Dean

Govt. Stanley College & Hospital

CERTIFICATE BY GUIDE

This is to certify that **DR. R.MEIRAJAN,** Post - Graduate Student (JULY 2013 TO APRIL 2016) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600001, has done this dissertation on **"STUDY ON CLINICAL, SEROLOGICAL, CYTOLOGICAL CORRELATION IN CASES OF AUTOIMMUNE THYROIDITIS"**

under my guidance and supervision in partial fulfilment of the regulations laid down by the TamilNadu Dr.M.G.R. Medical University, Chennai, for M.D.(General Medicine), Degree Examination to be held in April 2016.

Dr.G.RAJAN M.D

Professor

Department of Medicine

Govt. Stanley Medical

College & Hospital

Chennai 600001

DECLARATION

I **DR. R.MEIRAJAN** declare that I carried out this work on **"STUDY ON CLINICAL,SEROLOGICAL, CYTOLOGICAL CORRELATION IN CASES OF AUTOIMMUNE THYROIDITIS** at endocrinology OPD of Government Stanley Hospital during the one year period . I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other university, board either in India or abroad.

This is submitted to The TamilnaduDr.M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M. D. Degree examination in General Medicine.

Dr.R.MEIRAJAN

ACKNOWLEDGEMENT

At the outset I thank our Dean **Dr.ISAAC CHRISTIAN MOSES M.D,FICP,FACP** for permitting me to carry out this study in our hospital.

I express my profound thanks to my esteemed Professor and Teacher **Dr.R.JAYANTHI, M.D.,** Professor and HOD of Medicine, Stanley Medical College Hospital, for encouraging and extending invaluable guidance to perform and complete this dissertation.

I also express my profound thanks to my esteemed Professor and Teacher **Dr.G.RAJAN M.D.,** Professor of Medicine, Stanley Medical College Hospital, who is my unit chief for encouraging and extending invaluable guidance to perform and complete this dissertation

I wish to thank **Dr. CHANDRASEKAR,M.D., Dr.THILAGAVATHY, M.D.,** Assistant Professors of my unit, Department of Medicine, Stanley medical college Hospital for their valuable suggestions, encouragement and advice.

I sincerely thank the members of Institutional Ethical Committee, Stanley Medical College for approving my dissertation topic.

I thank all my Colleagues, House Surgeons, and Staff nurses and other para medical workers for their support.

Last but not the least; I sincerely thank all those **patients** who participated in this study, for their co-operation.

CONTENTS

ABBREVIATIONS

TSH- Thyroid stimulating hormone

FREE T3-Tri iodo thyronine

FREE T4-Thyroxine

SNG-Solitary Nodular Goiter

MNG-Multi Nodular Goiter

TPO-Antibody-Thyroid peroxidase antibody

FNAC-Fine needle aspiration cytology

INTRODUCTION

AUTOIMMUNE THYROIDITIS

- Auto immune thyroiditis is the condition where the immune system attack normal thyroid tissue.
- Hashimoto's thyroiditis or diffuse lymphocytic auto immune thyroiditis is the common form.
- It is the most common form of thyroiditis as well as most common cause of hypothyroidism in iodine sufficient areas.
- It is first described by a japanese surgeon Dr.Hakaru hashimoto in 1912.
- He coined the term struma lymphomatosa to the condition.
- The disease is characterised by pathological changes like lymphocytic infiltration, fibrosis, loss of follicular epithelium.
- The lymphocytic infiltration is a slow process so the symptoms of the disease may appear very late.
- The types of auto immune thyroiditis include goitrous thyroiditis, atrophic thyroiditis, juvenile thyroiditis, postpartum thyroiditis, silent thyroiditis, and focal thyroiditis.
- Goitrous form of auto immune thyroiditis is known as the hashimoto's thyroiditis.
- Its incidence is more among women than men.

TYPES OF AUTO IMMUNE THYROIDITIS

- **Goitrous thyroiditis** – manifest as swelling of thyroid gland with lymphocytic infiltration, fibrosis, thyroid cell hyperplasia.
- **Atrophic thyroiditis** – also known as primary myxedema. Usually manifest as atrophy and fibrosis of the thyroid gland.

  Both of them have a chronic course.
- **Juvenile thyroiditis** – shows lymphocytic infiltration. The disease have a chronic course but may disappear later during the life.
- **Post partum thyroiditis** – it shows a transient course and present as a small goiter with lymphocytic infiltration.
- **Silent thyroiditis** – painless thyroiditis with transient course. manifest as a small goiter and lymphocytic infiltration.
- **Focal thyroiditis** – can show a progressive course. It is present in thyroid gland of 20% of people at autopsy.

Eventhough the course and presentation of these types may vary the etiopathogenesis of each remain almost same.

A combination of genetic, hormonal, environmental, and other factors are responsible for the pathogenesis behind each of the auto immune thyroiditis forms mentioned above.

INCIDENCE and **PREVALENCE**

- Annual incidence of auto immune thyroiditis is 4/1000 women and 1/1000 men.
- Japanese populations most commonly affected.
- In those [japan] regions, genetic factors and chronic exposure to high iodine diet are important risk factors for auto immune thyroiditis.
- Sub clinical hypothyroidism found in 6-8% of women and 3% of men.
- Sub clinical hypothyroidism with auto antibodies transformed into hypothyroidism is about 4%.
- Mean age group of auto immune thyroiditis 30-50 years .

AUTO IMMUNE THYROIDITIS IN INDIA

Studies conducted in indian population regarding auto immune thyroiditis shows that 16.7% of adults are having anti TPO antibody and about 12.5% have anti thyroglobulin antibodies. Studies conducted among the school going female students shows that 7.5% are juvenile auto immune thyroiditis which include both hashimoto's thyroiditis and focal lymphocytic thyroiditis. Further FNAC studies done among them shows that 15% of them are having subclinical hypothyroidism and 6.5% are having overt hypothyroidism.

ETIOLOGY

- The causes of hashimoto's thyroiditis are multifactorial. Family history among the hashimoto's thyroiditis patients suggest that it has a genetic predisposition and the higher incidence of the disease among women of perimenopausal age group suggest that it has also connection with some sex hormones.

- Pre existing auto immune conditions like type 1 diabetes mellitus, addison's disease etc are some of the risk factors for the development of hashimoto's thyroiditis.

- Environmental factors like infection, iodine, smoking, pregnancy, stress etc also play some role in the etiopathogenesis of autoimmune thyroiditis.

- Postpartum autoimmune thyroiditis can be resulted due to the effects of hormones or it can be due to intra thyroidal fetal microchimerism. Fetus can initiate an intra thyroidal allo immune reaction and which can precipitate autoimmune thyroiditis in pregnant women.

- Treatment with interferon gamma, IL-2 for cancer or hepatitis can cause worsening of the autoimmune process in person with existing subclinical autoimmune thyroiditis.

CLINICAL PRESENTATION

Hashimoto's thyroiditis can clinically present as symptoms associated with two primary complications of the disease – **diffuse goiter** and **hypothyroidism**. Rarely in some cases initially hyperthyroidism can develop which later become hypothyroidism as the disease progress. Sometimes the diffuse goiter presentation can be associated with euthyroid state also. So the exact diagnosis and identification of the disease and its clinical presentation are necessary for the treatment of the disease and better prognosis.

On diffuse goiter presentation the swelling is firm, lobulated with varying sizes. The lobulated appearance may be misdiagnosed as a multi nodular goiter. As the size of the goiter increases it can cause pressure symptoms such as dyspnoea, dysphagia, hoarseness of voice etc.

Sometimes the swelling can be painful due to increased blood flow to the thyroid gland. This can be misdiagnosed as a thyroid lymphoma.

PATHOGENESIS

After an insult in susceptible individuals tolerance of cells to the t lymphocytes is lost and an auto immune process triggers. Thyroid specific auto antigens are presented to the antigen presenting cells by the thyrocytes. The thyroglobulin produced in the thyroid tissue has a major role in the pathogenesis of autoimmune thyroiditis. Thyroglobulin possess almost 40 epitops and in autoimmune thyroiditis patients these epitope recognition patterns show some alterations from the normal individual. Thyroid peroxidase enzyme also has significant role in pathogenesis because studies have showed that almost 180 auto antibodies are present against TPO enzyme and they cause more immunological damage to the thyroid tissue than other auto antibodies. Lymphocytic infiltration of the gland occurs in central stages of the disease.

Finally the glandular cells are destructed by the cytotoxic activity of the T cells, apoptotic activity of the antibodies produced from B lymphocytes and cytokine activity produced by the macrophages. Finally the patient develop hypothyroidic features.

INVESTIGATIONS

- **Thyroid function tests (TFT)**
- **anti TPO antibodies are positive.**
- **FNAC – shows presence of hurthle cells.**

THYROID FUNCTION TEST

The hormone levels produced by the thyroid and pituitary glands are estimated in this test. TSH, free T4, free T3 values are determined and the thyroid status of the patient is detected. So treatment can be given based on the thyroid status.

Anti TPO antibody test

This is an antibody test where the presence of anti TPO antibodies in the blood is detected. Its presence in blood confirms the diagnosis of hashimoto's thyroiditis.

FNAC OF THYROID

FNAC and further staining study of the sample shows heterogenous lymphocytic infiltrations and presence of hurthle cells.

TREATMENT

Thyroid hormone replacement therapy

Synthetic thyroid hormones or natural extracts containing thyroid hormones can be used for treatment of hashimoto's thyroiditis.

Synthetic thyroid hormones are levonyl, synthroid, levothroid etc.

Natural extracts containing thyroid hormones are produced from the pigs.

Ex: Armor thyroid which contain both levo thyroxine and tri iodo thyronine.

PROGNOSIS

Excellent prognosis with early diagnosis and proper treatment.

PREVENTION

Since it is an auto immune disorder it is difficult to prevent and till now no effective prevention method is discovered.

AIM OF THE STUDY

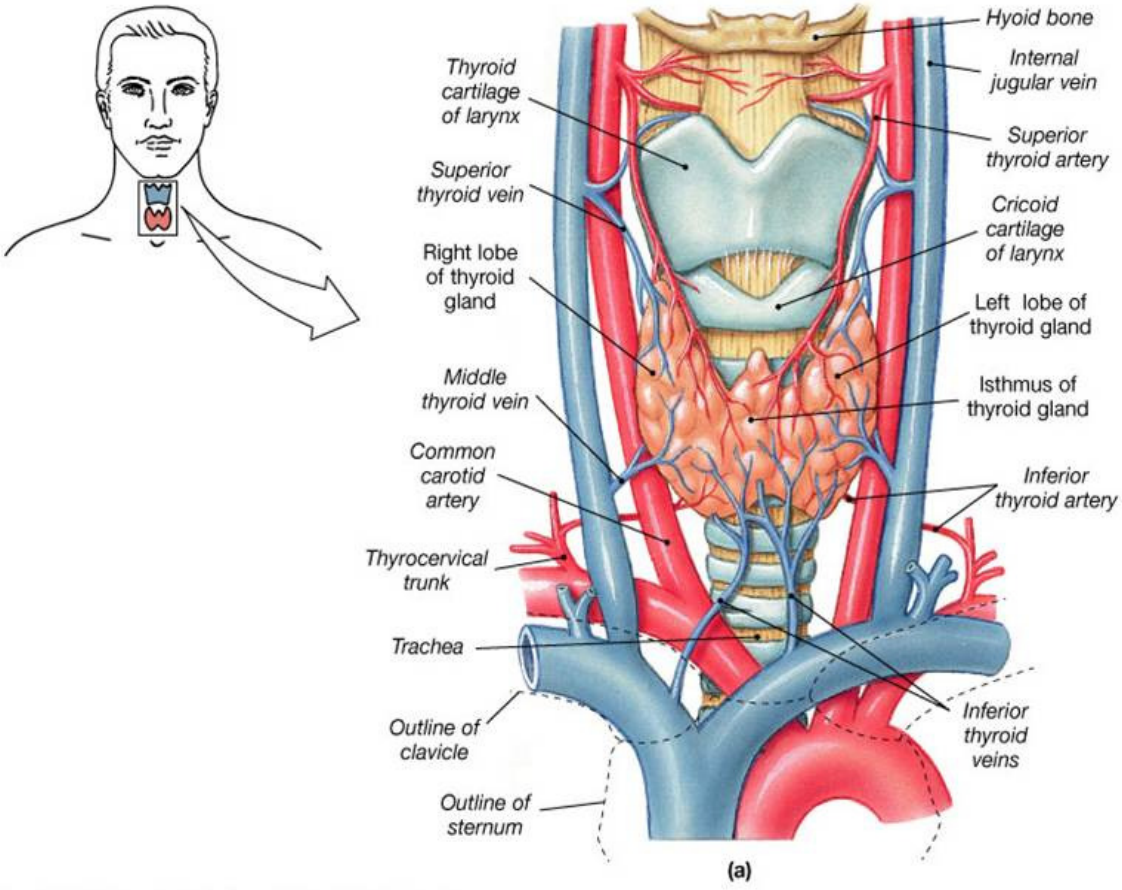
AIM AND OBJECTIVES

1. **To study the frequency of auto immune thyroiditis, mode of presentation, to determine the age and sex incidence.**
2. **To find out the correlation between auto antibodies, thyroid hormones, and cytological features in auto immune thyroiditis patients.**

REVIEW OF LITERATURE

THYROID GLAND

Thyroid gland is a butterfly shaped gland located in the anterior part of neck and consists of two lobes – right and left lobes those are connected together by a small lobe called the isthumus. A third lobe called pyramidal lobe may project from the isthumus. Sometimes a fibromuscular band known as levator glandulae thyroidae is seen in some individual from hyoid bone to the pyramidal lobe or isthumus.



SITUATION

Thyroid gland is situated against C5,C6,C7 and T1 vertebrae. each lobe extend from middle of thyroid cartilage to the fourth or fifth tracheal ring. Isthumus extend from second tracheal ring to fourth tracheal ring.

MEASUREMENTS

One lobe almost 5x2.5x2.5 cm in size. isthumus around 1.2x1.2 cm. thyroid gland weighs about 25grams. size of the thyroid is larger in females than males. during the periods of menstruation and pregnancy the gland may increase in size.

CAPSULES OF THYROID GLAND

It has two capsules-a true and false capsules.

True capsule – formed by the condensation of the outer connective tissue of the gland. Deep to the true capsule a capillary plexus is seen.

False capsule – formed from the pre tracheal layer of the deep cervical fascia. It forms a ligament known as suspensory ligaments of berry that connect the gland to the cricoid cartilage.

PARTS OF THYROID GLAND

Each lobe possess – an apex, a base, three surfaces – lateral, medial, posterolateral and two borders - anterior and posterior.

ARTERIAL SUPPLY

Thyroid gland is supplied by the superior and the inferior thyroid arteries.

Superior thyroid artery is the first anterior branch

of external carotid artery. It divides into anterior and posterior branches at the upper pole of thyroid gland.

One side anterior branch anastamose with the same of the opposite side and the posterior

branch anastamose with the ascending branch of

inferior thyroid artery.

Inferior thyroid artery is a branch of subclavian artery from the thyro cervical trunk. It divides into four to five glandular branches.

Tracheal and esophageal arteries give rise to some accessory thyroid arteries that also supplies the thyroid gland.

VENOUS DRAINAGE

Superior, middle, and inferior thyroid veins perform the major venous drainage from the thyroid gland.

Superior thyroid vein drains the upper portion and joints with the internal jugular vein.

Middle jugular vein also joints with the internal jugular vein.

Inferior thyroid veins drains from lower portions of thyroid and enters left brachiocephalic vein.

Kocher's vein – 4^{th} thyroid vein seen in some individual.

LYMPHATIC DRAINAGE

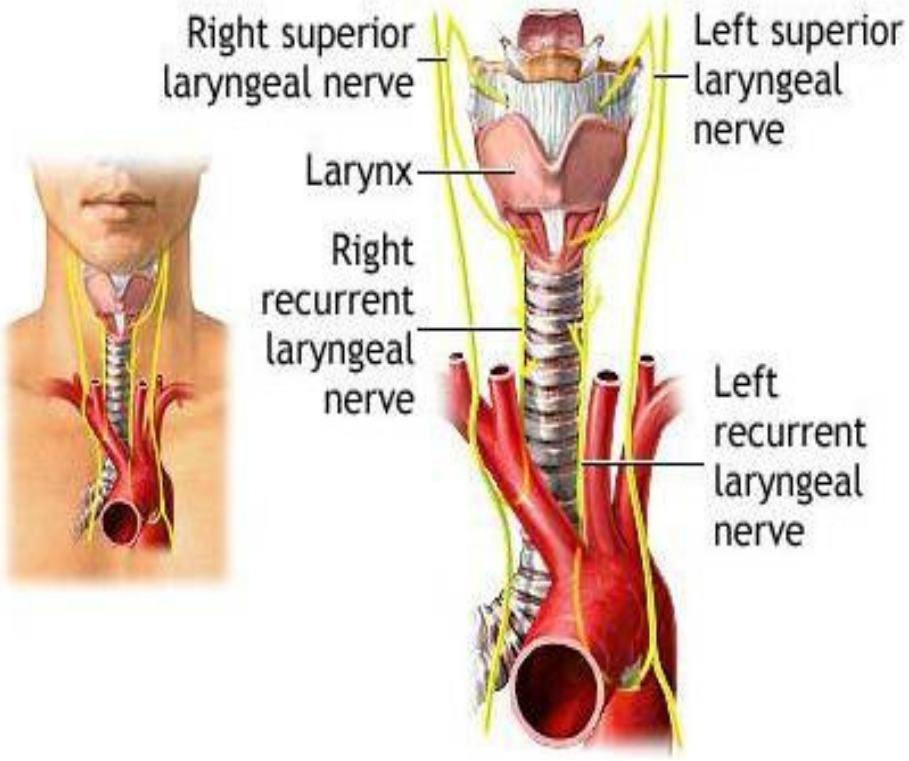
Lymphatic drainage from upper portions of the gland goes to deep cervical lymph nodes.

Lymphatics from lower portions of the gland drains to lower deep cervical lymph nodes.

NERVE SUPPLY

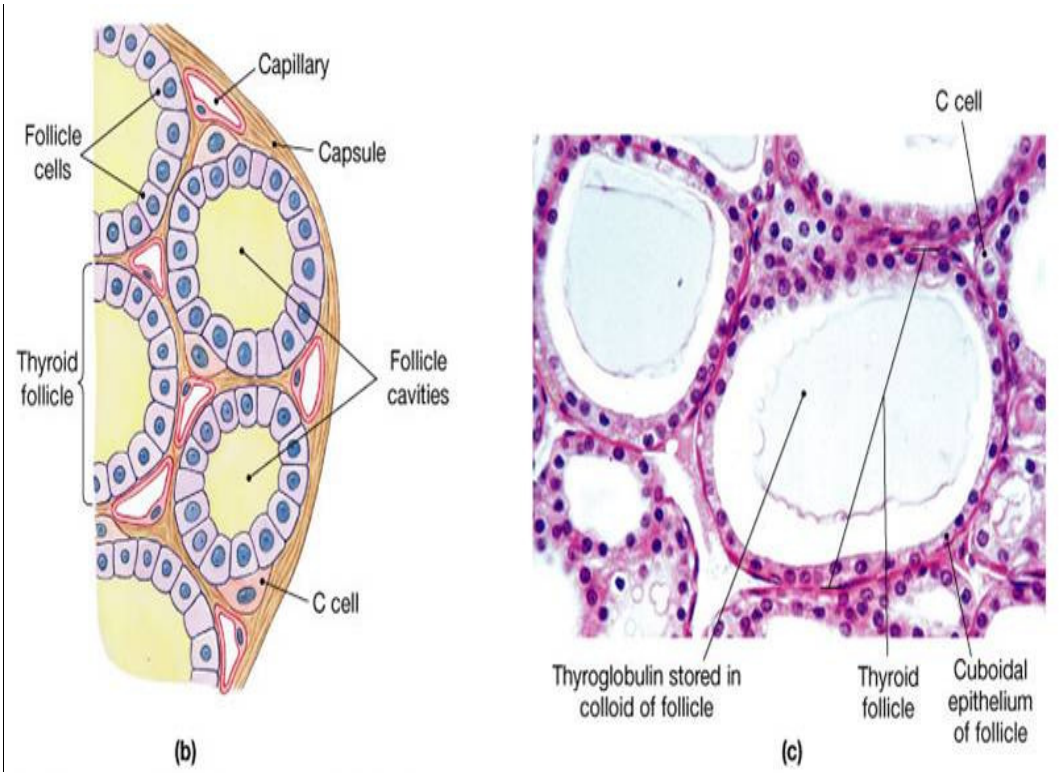
Major nerve supply derives from middle cervical ganglia. superior and inferior cervical ganglia also take part in nerve supply to thyroid gland.

Para sympathetic fibers derived from vagus nerve.



HISTOLOGY OF THYROID GLAND

Histologically it consists of two type of cells – follicular and parafollicular cells. Follicular cells secretes T3 and T4. The lining epithelium of the follicular cells are columnar during secretary phase and cuboidal during inactive phase. The follicular cells store its secretions as colloid inside it. Thyroid also contain parafollicular cells or C cells which are distributed in between the follicular cells. They secrete calcitonin hormone which has role in calcium metabolism.



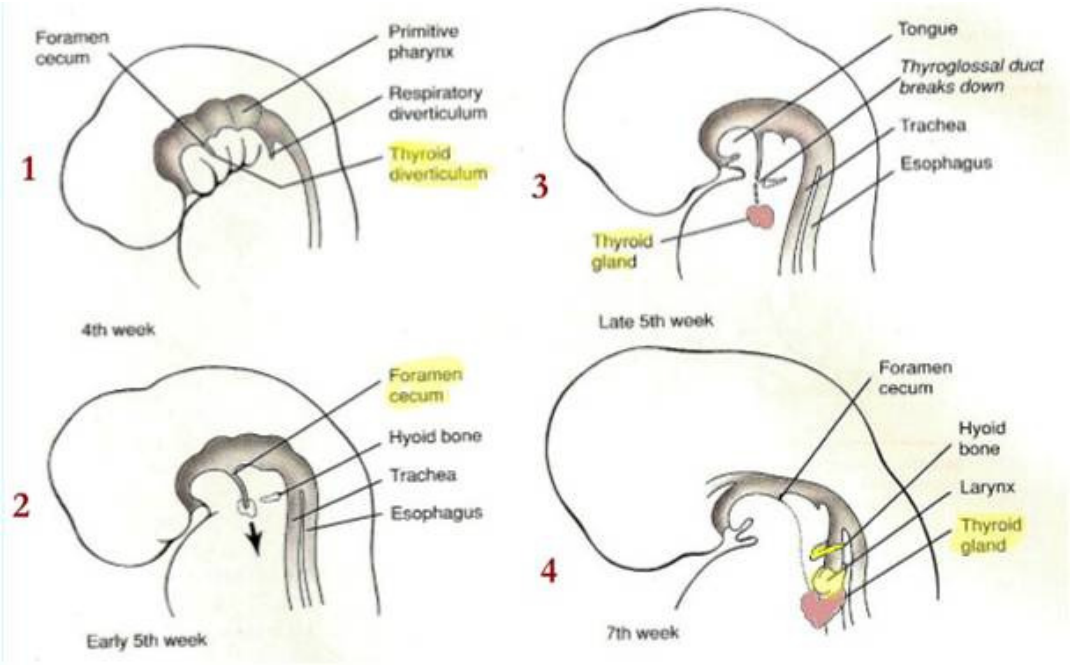
DEVELOPMENT OF THYROID GLAND

Thyroid gland develop from a structure known as the median endodermal thyroid diverticulum. This diverticulum grows downwards from the floor of the primitive pharynx caudal to tuberculum impar.

Thyroid gland is formed by the enlargement of the lower end of the diverticulum. The remaining part of the diverticulum remains as a narrow structure known as the thyroglossal duct.

Upper end of diverticulum is represented by the foramen caecum of the tongue and the lower end is represented by the pyramidal lobe.

The thyroid gland become functioning from the third month of development.



THYROID – PHYSIOLOGY

The follicular cells of the thyroid gland secrete tri iodo thyronine (T3) and tetra iodo thyronine (T4 or thyroxine). They regulate the basal metabolic functions of the body. T3 and T4 secretions are regulated by the thyroid stimulating hormone (TSH) produced from the anterior pituitary gland. Para follicular cells of the thyroid gland secrete another one hormone called calcitonin. It regulate the calcium metabolism of the body.

About 93% of the active hormone secreted by the thyroid is thyroxine and remaining 7% is tri iodo thyronine. But in the tissues most of the T4 secreted are converted to tri iodo thyronine. So both of these are functionally important.

Both the hormones have almost same functions but the rate and intensity of the activities differs. Tri iodo thyronine is almost four times more potent than thyroxine but its half life and concentration in blood are less.

CALCITONIN – it is a peptide hormone secreted by the para follicular cells of thyroid. Its function is to reduce plasma concentration of calcium.

SYNTHESIS AND SECRETION OF THYROID HORMONES

IODINE REQUIREMENT

The first step of thyroid hormone synthesis starts from the transport of iodides from the blood into the thyroid cells and follicles. This is process known as IODIDE TRAPPING.

Iodide trapping is done by the basal membrane of the cells of the thyroid gland which shows 250 times greater ability than other cells for thyroid transport.

A very important factor which regulate the rate of the iodide trapping is TSH concentration.

TSH stimulates the activity of the thyroid pump in the thyroid cells. Specific membrane receptors called TSH receptors are present in thyroid cells for its functioning. The TSH receptor is G protein coupled receptor.

STEPS OF SYNTHESIS

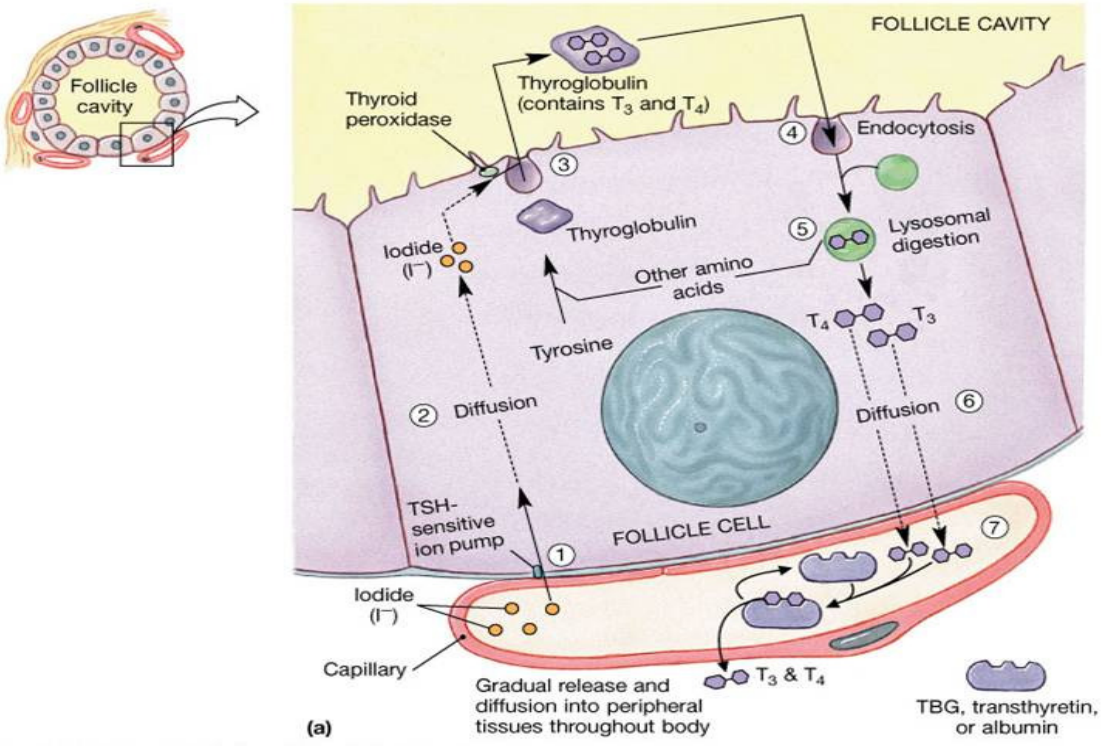
1. Iodide trapping

2. Thyroglobulin formation and secretion

3. Oxidation of the iodide ion

4. Iodination of thyronine and formation of thyroid hormones

5. Storage of thyroglobulin.



THYROGLOBULIN FORMATION

The endoplasmic reticulum and the golgi apparatus of the thyroid cells produce a large molecular weight glycoprotein called THYROGLOBULIN. Tyrosine amino acid is an essential substrate for the production of thyroglobulin. Each molecule of thyroglobulin contain almost 70 tyrosine amino acids.

The thyroxine and the tri iodo thyronine are almost an integral part of the thyroglobulin molecule during synthesis and during storage also.

OXIDATION OF THE IODIDE ION

The trapped iodides are oxidised at the apical membrane of the thyroid gland with the help of a peroxidase enzyme and hydrogen peroxide to nascent iodine (oxidised iodine).

IODINATION OF TYROSINE

Iodination of tyrosine is also known as organification of thyroglobulin.

one molecule of oxidised iodine is added to thyroglobulin to produce mono iodo thyronine and then one more molecule is added to form di

iodo thyronine. Then one di iodo thyronine get coupled with mono iodo thyronine or another one molecule of di iodo thyronine to produce tri iodo thyronine or thyroxine respectively.

This is a slow process but it is activated by an enzyme iodinase present in the thyroid cells.

The major hormonal product of the coupling reaction is the thyroxine.

Both thyroxine and tri iodo thyronine remains as a part of the thyroglobulin molecule itself.

STORAGE OF THYROGLOBULIN

Thyroid gland is capable of storing huge amount of T3 and T4 after production for future body requirements.

RELEASE OF T4 AND T3

The apical surface of the thyroid cells forms pinocytic vesicles around the colloid of follicular cells by a pseudopod extension. Then lysosomes of cytoplasm immediately fuse with these vesicles. Proteases present in the lysosomes degrade the thyroglobulin molecule and release T4 and T3 in free form. Free T4 and T3 diffuses from thyroid cells to the

sorrounding capillaries. Thus the thyroxine hormones reaches the blood. About 93% is T4 and remaining is T3. But in the tissues about half of the T4 is deiodinated to additional tri iodo thyronine. So the tissues mainly uses tri iodo thyronine.

TRANSPORT OF T4 AND T3

When released into blood T4 and T3 bind with plasma proteins like thyroid binding globulin and thyroid binding pre albumin. T4 shows greater affinity and T3 shows lesser affinity to these plasma proteins. So T4 is delivered slowly and T3 is delivered rapidly to the tissues. Inside the tissue cells also T4 shows more affinity to bind with the intra cellular proteins. So T3 is used up very early by the tissues and T4 is stored for longer duration.

Since the thyroid hormones show affinity to intracellular proteins they are having long latent period of action (slow onset and longer duration of action). The actions of T3 occur about 4 times rapidly than T4 with a latent period of 6 to 12 hours and peak cellular activity with in 2 to 3 days.

COMPARISON BETWEEN T4 AND T3

T4	T3
Thyroid secretes more amount of T4(tetra iodo thyronine).	Secrete less amount of T3(tri iodo thyronine) when compared to T4.
More tightly bound to plasma protein.so it is the circulating form.	Less tightly bound to plasma protein. so less circulation.
Slow acting form. Peak effect only after 6 to 8 days.	T3 is five times more potent than T4. So faster action.
Less bound to nuclear receptors. T4 receptor complex is unable to activate or depress the gene transcription.	More avidly bound to nuclear receptors. So this complex can regulate transcription process.
One third of T4 is converted to T3 in thyroid, liver, kidney by the type 1 deiodinase enzyme. So it is the secretary form.	Target cells usually generates T3 by type 2 deiodinase enzyme. So it is the active form.

FUNCTIONS OF THYROID HORMONES

1. Increases the transcription of many genes.

   Thyroid hormones activates nuclear receptors and this increases the rate of many transcription processes.

2. Increases cellular metabolic activity.

   Thyroid hormones increases the size, number and activity of the mitochondria. This increases the rate of ATP production and accelerates cellular function.

3. Thyroid hormone increases the Active transport of ions through cell membranes by activating Na+ K+ ATPase pump. This can cause increase in body heat production.

4. Effects on growth.

   Growth and development of the brain during the fetal life and initial few years of the life are promoted by the thyroid hormones.

5. Stimulate various carbohydrate metabolism like enhancement of absorption from GIT, uptake by cells, glycolysis, gluconeogenesis, increased insulin secretion etc.

6. Enhancement of fat metabolism.
7. Plasma levels of cholesterols, phospholipids, triglycerides are decreased by thyroxine.
8. Cholesterol, triglycerides and phospholipid levels are increased by thyroxine in liver causing excess fat deposition in liver.
9. Relative vitamin deficiency occur due to excess thyroxine because of the increased activity of many enzymes.
10. Increased basal metabolic rate.
11. Increases respiration.
12. Increased gastro intestinal motility.
13. Increased thyroid levels can cause nervousness and psycho neurotic tendancies.
14. Increased thyroxine can cause muscle weakness due to excess protein catabolism.
15. Increased levels can cause fine muscle tremors due to increased reactivity of the neuronal synapses in the areas of the spinal cord that control muscle tone.

16. If thyroid excess sleeping difficulty occurs eventhough tiredness is present.

17. Effect on cardio vascular system

- Blood flow and cardiac output increases.
- Increased heart rate.
- Maintain normal arterial pressure.
- Increased heart strength.

18. Effect on other endocrine glands

- Increases insulin secretion by pancreas.
- Increases para thyroid hormone secretion.
- Increases ACTH production by pituitary thereby increases glucocorticoid secretion by adrenal.

19. Effect on sexual activity

- In man – excess thyroxine can cause impotence and decrease can cause loss of libido.
- In women – thyroid hormone abnormalities can cause menstrual irregularities.

REGULATION OF THYROID HORMONE SECRETION

Thyroid secretion is maintained by some specific feedback mechanisms acting via the hypothalamus and anterior pituitary glands.

ROLE OF TSH (THYROTROPIN)

- Increases the proteolysis of the thyroglobulin that has stored in the follicles and releases the thyroid hormones to the blood.
- Activation of iodide trapping mechanism.
- Increases iodination of tyrosine amino acid.
- Increases the size and activity of the thyroid cells.
- Helps in transformation of cuboidal epithelium to secretory columnar epithelium.

ROLE OF CYCLIC AMP IN TSH ACTIVITY

First step of TSH activity is binding with specific TSH receptors on the basal membrane surface of the thyroid cells. It activates adenyl cyclase in the membrane and this increases the formation of the cyclic AMP inside the cell. Cyclic AMP act as a second messenger for the activation of protein kinase enzymes. As a result of the activity of protein kinase enzymes phosphorylation occur throughout the cells and proteolysis of thyroglobulin is achieved and thyroxine and tri iodo thyronine are released.

ROLE OF TRH IN RELEASE OF TSH

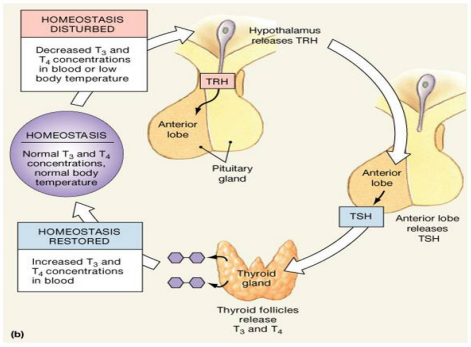
TRH is the thyrotropin releasing hormone secreted by the hypothlamus. Secreted TRH molecules reaches the anterior pituitary through the hypothalamo – hypophysial portal blood system. TRH directly increases the TSH output from anterior pituitary. The molecular mechanism of this process also mediated by the activity of some secondary messengers like phospholipase C, calcium ions, diacyl glycerol which eventually leads to TSH release.

FACTORS INFLUENCING TRH RELEASE

- Exposure to cold can cause increase in secretion of TRH from hypothalamus.
- Various emotional reactions like anxiety, excitement can stimulate the sympathetic nervous system and cause decrease in secretion of TRH.

FEED BACK MECHANISAM OF THYROID HORMONE SECRETION

An increase in thyroid hormone levels in body causes reduction of TSH secretion from the anterior pituitary. This happens as a direct effect of thyroid hormone levels over the anterior pituitary gland itself. This suggest the TSH release from anterior pituitary obeys a feed back mechanism.



ANTI THYROID SUBSTANCES

- Thiocyanate ions – decreases the iodide trapping.
- Propyl thio uracil, methimazole, carbimazole prevent the formation of thyroid hormones from iodides and tyrosine.
- Iodides in higher concentrations can decrease thyroid activity and thyroid gland size.

DISORDERS OF THYROID

1.HYPERTHYROIDISM

2.HYPOTHYROIDISM

3.CRETINISM

HYPERTHYROIDISM

CAUSES

- Graves' disease
- Auto immune thyroid diseases
- Hashitoxicosis
- Toxic adenoma
- Toxic MNG
- TSH mediated hyperthyroidism

In all the above cases the thyroid shows high uptake of iodine in radio iodine uptake study.

- Subacute thyroiditis
- Ectopic hyperthyroidism
- Metastatic follicular thyroid cancer
- Drugs (amiodarone, excess of iodine)

These cases show hyperthyroidism with low iodine uptake in radio iodine uptake study.

In hyperthyroidism the TSH levels are decreased and the thyroid gland shows enlargement.

In autoimmune cases of hyperthyroidism auto antibodies known as thyroid stimulating immunoglobulins (TSI) are present in blood. They exert actions similar to those of TSH and causes hyperthyroidism.

SYMPTOMS

- Higher excitability state
- Intolerance to heat
- Increased sweating
- Weight loss
- Diarrhoea
- Muscle weakness
- Nervousness or other psychic disorders
- Fatigue and tiredness
- Inability to sleep
- Fine hand tremors

- Many patients show exophthalmus

INVESTIGATIONS

- Serum T3 and T4 are elevated.
- TSH levels are low in primary thyrotoxicosis.
- TSH receptor antibodies are elevated in grave's disease.
- Radio iodine uptake studies
- Thyroid ultra sound scanning – can identify nodules.

MANAGEMENT OF HYPERTHYROIDISM

- Anti thyroid drugs – propyl thio uracil, methimazole, carbimazole.
- Radio active iodine – iodine 131 is used in treatment of hyperthyroidism. Radio active iodine therapy is contraindicated during pregnancy.
- Surgical therapy
- Symptomatic treatment – a non selective beta blocker like propranalol or nadolol is used for symptomatic treatment. This is helpful for controlling symptoms such as such as tachycardia, palpitations, tremors.

GRAVE'S DISEASE

Grave's disease consists of the triad of hyperthyroidism, goiter, ophthalmopathy.

Sometimes a condition known as infiltrative dermopathy or pre tibial myxedema can also occur along with grave's disease.

CAUSE – auto antibodies are produced by B lymphocytes against TSH receptors. These auto antibodies activate the receptors. As a result of this thyroid hormone synthesis is increased and hyperthyroidic features develop. Genes associated with the pathogenesis of grave's disease are HLA B8, DR3, DR2.

Immunological activation of fibroblast in extra occular muscles and skin are causing accumulation of glycosaminoglycans and results in ophthalmopathy and dermopathy. Ophthalmopathy causes lid retraction, proptosis and other eye signs of grave's disease.

Dermopathy is the accumulation of hyaluronic acid in the dermis. Mucinous edema and fragmentation of collagen fibers are the changes occuring in skin and producing papules or macules. Pre tibial areas of the lower leg is the most commonly affected.

THYROTOXIC CRISIS

Thyrotoxic crisis or thyroid storm is a life threatening condition where the thyrotoxic features become very severe and it is a medical emergency.

PRECIPITATING FACTORS – trauma, infection, radio iodine therapy, sub total thyroidectomy in an improperly prepared patients.

FEATURES

- Hyper pyrexia
- Agitation, confusion, psychosis
- Atrial fibrillation, tachycardia
- Vomiting, diarrhoea, jaundice, hepatic failure.

TREATMENT

- Rehydration
- Antibiotics
- Beta blockers – to control sympathetic activity
- Sodium ipodate, carbimazole
- Glucocorticoids – reduce conversion of T4 to T3.

HYPOTHYROIDISM

TYPES

1. Primary hypothyroidism
2. Secondary hypothyroidism
3. Thyroid hormone resistance

CAUSES OF PRIMARY HYPOTHYROIDISM

- Chronic auto immune thyroiditis
- Iatrogenic (after thyroidectomy)
- Iodine deficiency
- Drugs like lithium, thionamides, amiodarone
- Congenital causes like thyroid dysgenesis

CAUSES OF SECONDARY HYPOTHYROIDISM

- TSH deficiency
- TRH deficiency

Deficiency of the above to regulatory hormones are the major cause.

SYMPTOMS

- Fatigue and sleepiness
- Muscular weakness
- Slowed heart rate
- Increase in body weight
- Constipation
- Reduction in cardiac output and blood volume.
- Mental sluggishness
- Reduced hair growth
- Scaliness of skin
- Voice becomes husky
- Severe cases produces a generalised edematous condition known as myxedema.

INVESTIGATIONS

- Serum T4 is low
- Serum T3 is low

- Serum TSH levels are elevated

MANAGEMENT

Levo thyroxine is used for the treatment of hypothyroidism.

Treatment aims the attainment of euthyroid status.

Dose – 50 to 200 micrograms/day.

CRETINISM

Cause – hypothyroidism in fetal life, infancy, or childhood. This can be due to congenital lack of thyroid gland (congenital cretinism), or genetic defect in thyroid gland which impairs thyroxine production, or iodine lack in the diet (endemic cretinism).

Features – mental retardation and growth retardation. Skeletal growth is more inhibited than soft tissue growth. Excessive growth of soft tissues can result in obese, short, stocky child.

Treatment – iodine or thyroxine. Treatment should be given with in a few weeks of birth.

GOITRE

SIMPLE GOITRE

- Diffuse enlargement of the thyroid.
- When enlarged follicles filled with colloid it is known as colloid goiter.
- Commonly affects the age group 15 to 25 years.
- Patient is in euthyroid state and may regress.
- **Endemic goiter** – seen in areas of iodine deficiency. So it can be prevented by providing adequate amounts of iodine in the diet and iodised oil injection once in two years.

MULTI NODULAR GOITRE

- Multi nodular enlargement of the thyroid
- Patient usually present with features of thyrotoxicosis

THYROIDITIS

Based on duration

- Acute
- Sub acute
- Chronic

Based on etiology

- Auto immune – hashimoto's thyroiditis
- Granulomatous – de quervains thyroiditis (post viral inflammatory response – painful thyroiditis)
- Fibrosing thyroiditis – Riedel's thyroiditis
- Infective – acute (bacterial and viral)

  Chronic (tuberculous, syphilitic).

DIAGNOSIS OF THYROID DYSFUNCTION

1. **Thyroid function tests(TFT)**

- Serum TSH – 0.5 to 5 micro units/L

- Free T4 – 12 to 28 picomols/L
- Free T3 – 3 to 9 picomols/L
- Total T4 – 50 to 150 nanomols/L
- Total T3 – 1.5 to 3.5 nanomols/L

TSH – decreased in hyperthyroidism and central hypothyroidism.

Total T4 – its levels reflect the output from the thyroid gland.

Total T3 – indicates the peripheral thyroid metabolism.

Free T4 and T3 – normal in euthyroidism, high in hyperthyroidism and low in primary hypothyroidism.

2. **Thyroglobulin level** - <1 to 35 micro grams/L
3. **USG neck** – to differentiate the swelling (cystic or solid, SNG or MNG)
4. **FNAC** – to detect colloid goiter, auto immune thyroiditis and malignancy.
5. **Radio active iodine uptake study**

- Normal uptake – 16 to 48%

- Hyperthyroidism - >48% uptake
- Hypothyroidism - <15% uptake

6. **Thyroid scan** – a radio active substance that concentrates in thyroid is taken orally or given iv and pictures of thyroid are taken using a gamma camera.

7. Uptake of radionuclide increased in

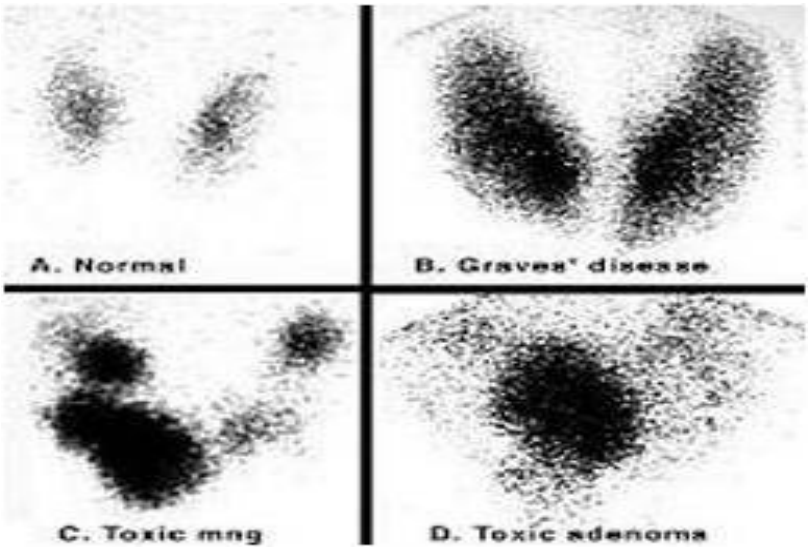
    1.Hyperthyroidism

    2.Early stages of Hashimoto's thyroiditis

8.Uptake of radionuclide decreased in

    1.Hypothyroidism

    2.subacute thyroiditis



AUTO IMMUNE THYROIDITIS

ETIOLOGY

- Genetic factors – it shows linkage with HLA class 1 and class 2, cytotoxic T lymphocyte associated antigen (CTLA 4 gene), and functional polymorphisms of protein tyrosine phosphatase 22 gene (PTPN 22 gene).
- Immunological factors – a pre existing auto immune disorder like type 1 diabetes mellitus can be a risk factor for the development of hashimoto's thyroiditis.
- Environmental factors – infection, iodine, smoking, pregnancy etc.

ROLE OF THE ETIOLOGICAL FACTORS

- MHC class 2 genes – they encode products which remove auto reactive T cells.
- CTLA 4 gene – they terminate T cell activation. So any change in this gene can cause uncontrolled T cell activation.
- PTPN 22 gene – codes for a T cell activation inhibitor.
- Infectious agents – they may produce auto antigens.

- Infectious agents can also alter the expression of the surface molecules, they can mimic as auto antigens and directly affect the immune system.

- Dietary factors – increased iodides in food can cause enhancement of immunogenicity of thyroglobulin, can alter thyroid cell function, and forms toxic metabolites with oxygen. Vitamin D deficiency can affect T cells and dendritic cells and it may predispose to auto immune diseases.

- Pollutants and toxins like ciggerete smoke, methyl cholanthrene may affect T cells and cytokines.

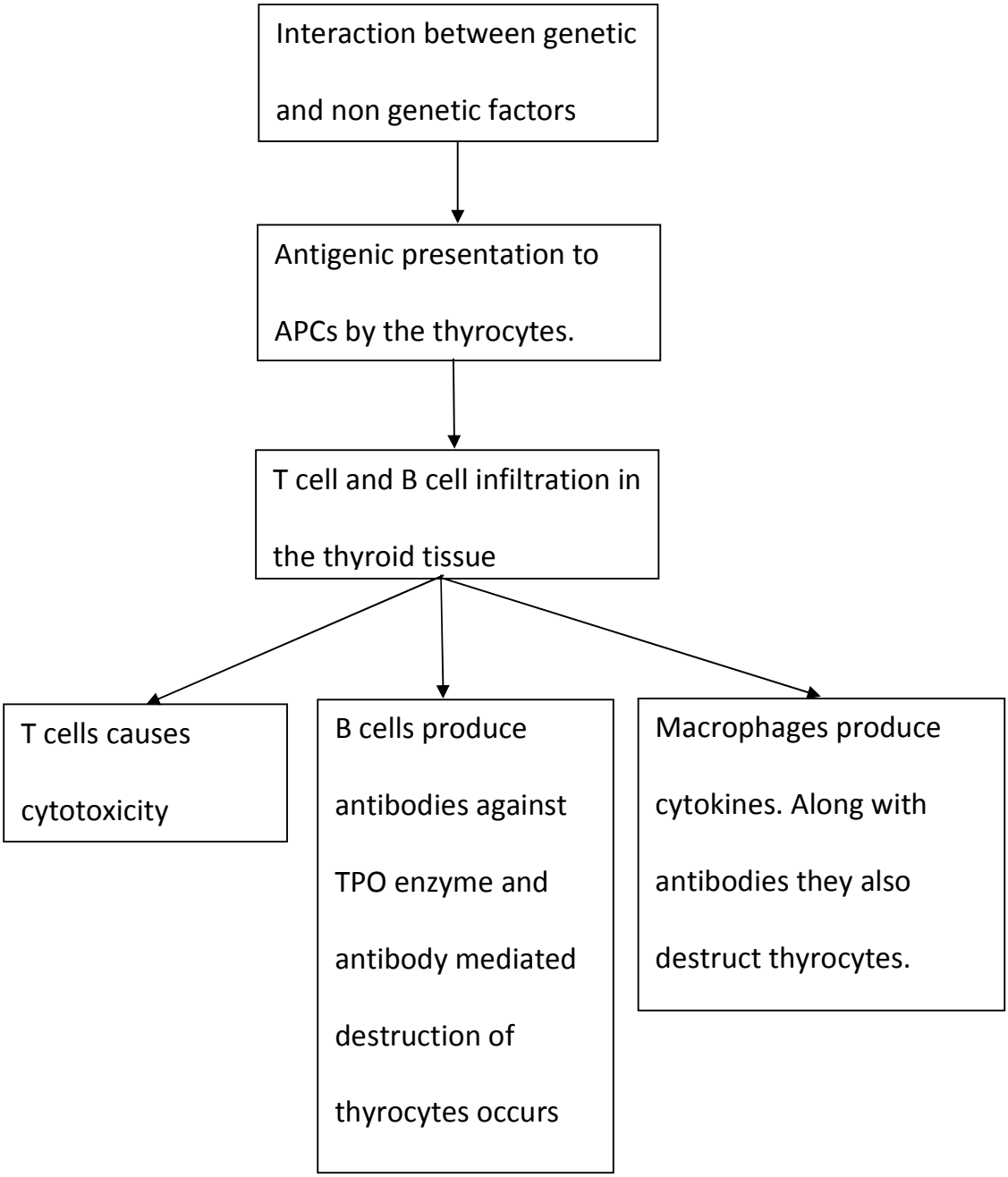
- Hormones – estrogen enhances the immune responses and androgens and gluco corticoids suppress the immune response.

- Stress – stress can alter the interaction between the neuroendocrine system and immune system. So this can be a predisposing factor.

- Drugs – lithium, interferon alfa, cytokines can potentiate the pathogenesis of auto immune thyroiditis.

- Bone marrow transplantation from an affected donor can cause immune reconstitution syndrome and this can favour the pathogenesis of auto immune thyroiditis.

PATHOGENESIS



Pathogenesis involve the interaction between the genetical, immunological, and environmental factors mentioned above.

- Exposure of genetically predisposed persons to environmental factors
- Invasion of thyroid by antigen presenting cells of MHC class 2
- This presents the auto antigens against thyroid to the immune system for processing
- The immune system produces auto reactive cells against thyroid tissue
- Formation, clonal expansion, and maturation of auto reactive cells and auto antibodies in response to the presented antigen.
- B lymphocytes produces anti thyroid peroxidase and anti thyroglobulin antibodies.
- Self reactive T cells infiltrate the thyroid gland.
- CD8+ cytotoxic T cell mediated cell death, CD4+ T cell mediated cytokine production(IFN gamma) and further cell death by cytokine, binding of anti thyroid antibody and further antibody dependant cell death occurs eventually.

- At the final stages caspases also cause thyroid destruction.

THYROID AUTO ANTIBODIES

- **Thyroid peroxidase antibodies** – major antibody seen in almost 90% patients of auto immune thyroiditis. It is mainly of Ig G type antibody.

- **Thyroglobulin antibodies** – seen in almost 60% of thyroiditis patients and 30% of grave's disease patients. They are also of immunoglobulin Ig G category.

- **Thyroid stimulating hormone receptor antibodies** – major auto antibody seen in grave's disease and atrophic thyroiditis. In grave's disease it stimulate TSH receptors and in atrophic thyroiditis it blocks TSH receptors.

- Sodium iodide ion symporter(NIS), antibodies to thyroid hormone, non specific auto antibodies against DNA are the some other thyroid auto antibodies.

LEVELS OF THYROID AUTO ANTIBODIES

TPO antibodies – less than 35 iu/ml is negative and more than 50 iu/ml is positive.

TG antibodies – less than 225 iu/ml is negative and more than 325 iu/ml is positive.

HISTOLOGICAL PICTURE

- Mononuclear inflammatory infiltrates containing lymphocytes and plasma cells.
- Germinal centers are well developed
- **Hurthle cells** – atrophied thyroid follicle lined by epithelial cells containing abundant eosinophilic cytoplasm are seen.
- Hurthle cells and heterogenous lymphocyte infiltration in an FNAC biopsy sample is diagnostic for hashimoto's thyroiditis.

CLINICAL COURSE

The clinical presentation can be hypothyroid, euthyroid, or hyperthyroid.

The most common clinical presentation is diffuse enlargement of the thyroid with features of hypothyroidism.

Hashitoxicosis – in some cases the disruption of thyroid follicles produces secondary release of thyroid hormones and can result in a transient thyrotoxicosis.

SYMPTOMS

Symptoms due to decreased metabolic rate

- Fatigue and weakness
- Increased sensitivity to cold
- Weight gain
- Constipation
- Cognitive dysfunction
- Growth and mental retardation in children

Symptoms due to protein accumulation

- Dryness of skin, nails and hair
- Hoarseness of voice
- Facial puffiness
- Peri orbital edema

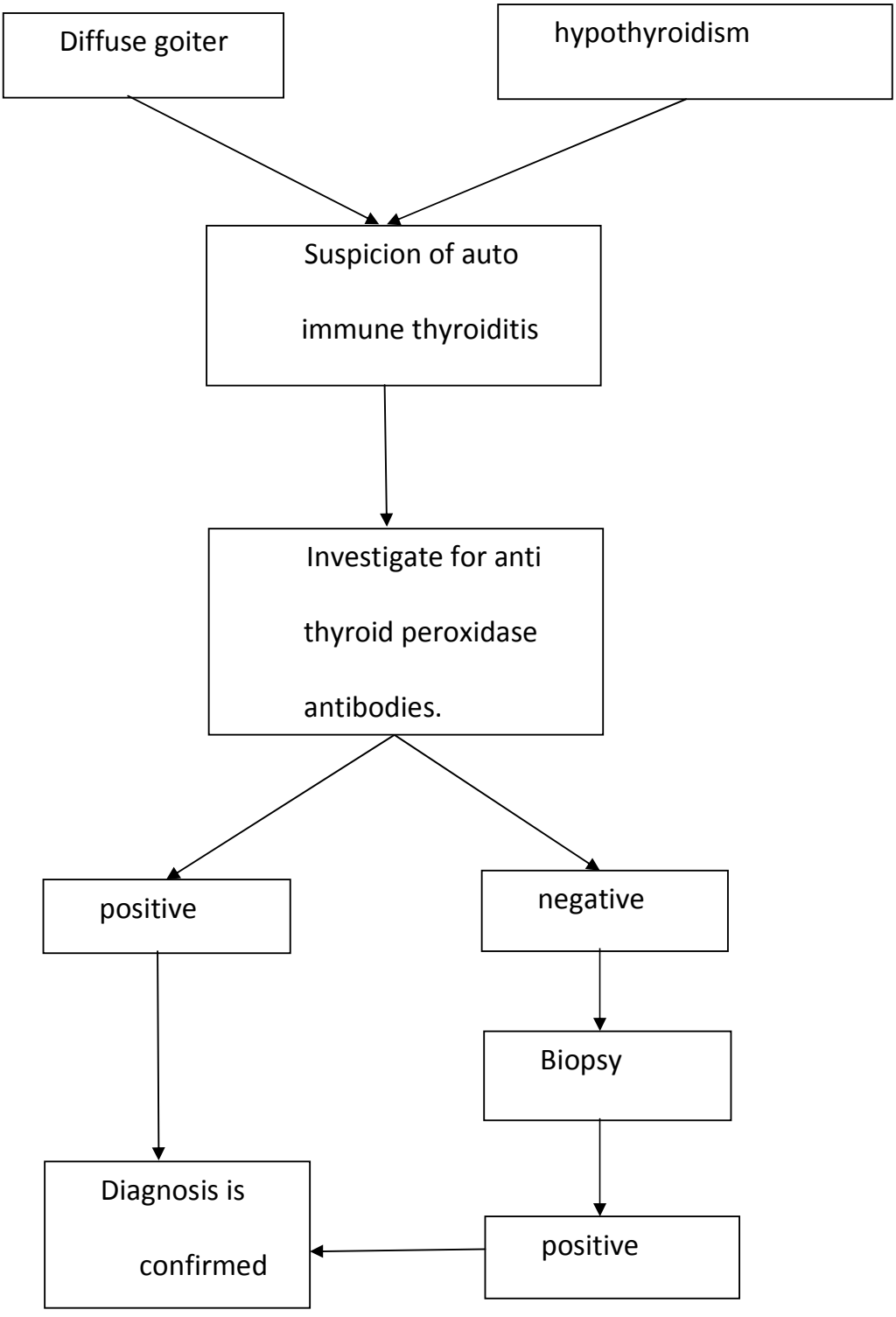
Other symptoms

- Depression
- Increased menstrual flow

- Myalgia
- Paraesthesia
- Arthralgia
- Pleural and pericardial effusions
- Pubertal delay
- Hearing abnormalities
- Diastolic hypertension
- Bradycardia
- Delayed tendon reflex relaxation

DIAGNOSIS

- **Thyroid function test(TFT)** – estimation of serum values of TSH, free T3, free T4 can be used to find the clinical picture.
- **Anti TPO antibody** - POSITIVE
- **FNAC** – Presence of hurthle cells and lymphocytic infiltration.


Diffuse goiter
hypothyroidism
Suspicion of auto immune thyroiditis
Investigate for anti thyroid peroxidase antibodies.
positive
negative
Biopsy
Diagnosis is confirmed
positive

TREATMENT

- If the patient presented with hypothyroidism, thyroxine replacement should be given.
- If the patient presented with euthyroidism, prophylactic thyroxine replacement should be given.
- If the patient presented with sub clinical hypothyroidism,we look TSH value .if the TSH value >10mU/L we give low dose thyroxine [starting dose 25-50micro gram/day].

INDICATIONS FOR SURGERY IN HASHIMOTO'S THYROIDITIS PATIENTS

- Patients presented with tracheal compression causing dyspnoea and esophageal compression causing dysphagia.
- Dominant mass unresponsive to thyroxine therapy.
- Increase in the size of the mass despite thyroxine therapy

COMPLICATIONS

- Diffuse goiter and hypothyroidism are the two primary complications of hashimoto's thyroiditis.
- Increased risk of other auto immune diseases like type 1 diabetes, autoimmune adrenalitis, rheumatoid arthritis, premature ovarian failure.
- Thyroid lymphoma – a very rare complication. Can appear as a nodule.
- Myxedema – can develop very rarely if hashimoto's thyroiditis is left untreated.
- Mental health issues like depression.
- Cardiac problems due to increased cholesterol.
- Hashimoto's encephalopathy.

HASHIMOTO'S ENCEPHALOPATHY

It is a rare complication occuring in hashimoto's thyroiditis. It is featured by a subacute onset of confusion which leads to delirium or dementia. The patient's thyroid status may be euthyroid but TPO antibodies are

positive. Now a days the condition is also called steroid responsive encephalopathy with auto immune thyroiditis(SREAT).

Clinical features

- Memory loss
- Seizures
- Ataxia
- Myoclonus

Investigations to do are thyroid function test, TPO antibodies, EEG etc.

MRI studies are usually normal but EEG shows non specific epileptiform discharges. CSF shows increased protein levels.

In general hashimoto's encephalopathy is a diagnosis of exclusion once psychiatric, infective, paraneoplastic, and vasculitic causes have been ruled out.

TREATMENT

The condition shows excellent positive response to high dose gluco corticoid therapy.

ASSOCIATED CONDITIONS IN AUTO IMMUNE THYROIDITIS

- Type 1 auto immune polyglandular syndrome – it include addison's disease, hypoparathyroidism.
- Type 2 auto immune polyglandular syndrome – type 1 diabetes mellitus, addison's disease, lymphocytic hypophysitis, vitiligo, alopecia, celiac disease, pernicious anemia, myasthenia gravis, premature ovarian failure.
- Rheumatological disorders such as rheumatoid arthritis, SLE, systemic sclerosis, sjogren's syndrome.
- Other conditions like auto immune thrombocytopenia, primary biliary cirrhosis, chronic active hepatitis can also occur with increased frequency in auto immune throiditis patients.

MATERIALS AND METHODS

SELECTION OF PATIENTS

- 100 cases of thyroid disease patients are selected from which 40 cases of auto immune thyroiditis patients are selected by using investigations like FNAC,TPO antibodies.

INCLUSION CRITERIA

- Clinical features and laboratory investigations proven thyroid disease patients .

EXCLUSION CRITERIA

- Patients with sick euthyroid syndrome
- Patients with thyroid malignancy
- Pregnant patients

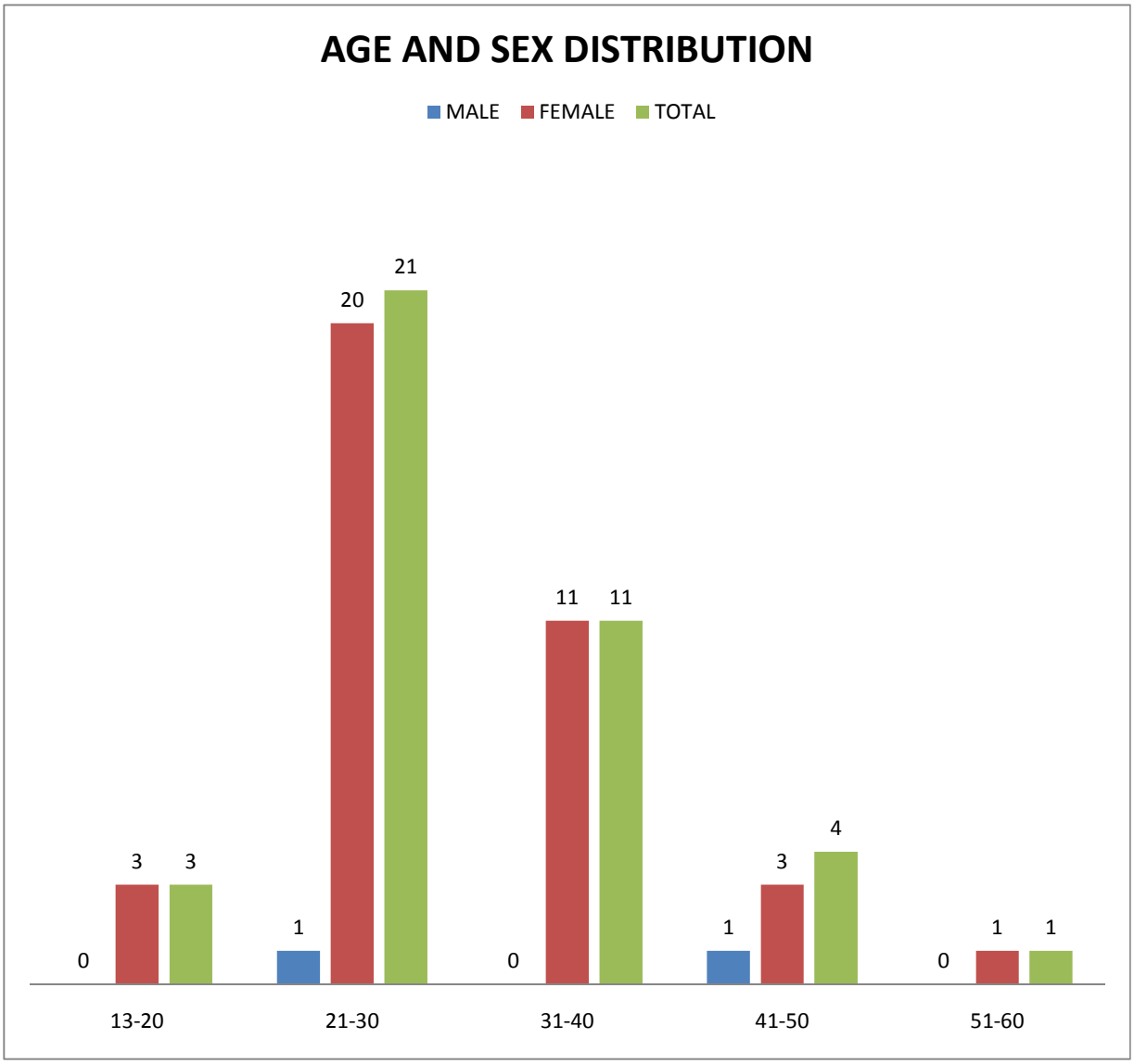
METHODOLOGY:

- This study is a cross-sectional study wherein 100 thyroid disease patients satisfying inclusion and exclusion criteria are selected from endocrinology OPD at Stanley medical college and informed consent obtained for enrolment in this study.
- Clinical features and laboratory investigations proven thyroid disease patients are selected wherein correlation of clinical and laboratory features like TFT,TPO-antibodies, cytology for these patients to be ascertained for autoimmune thyroiditis
- Statistics will be done for all data and suitable statistical tests of comparison will be done.
- Continuous variables will be analyzed with the unpaired t-test and categorical variables will be analyzed with the chi-square test with Yates correction.
- Statistical significance will be taken as $P< 0.05$.The data will be analyzed using EpiInfo software (7.1.0.6version:Center for disease control, USA) and Microsoft Excel 2010.

OBSERVATION

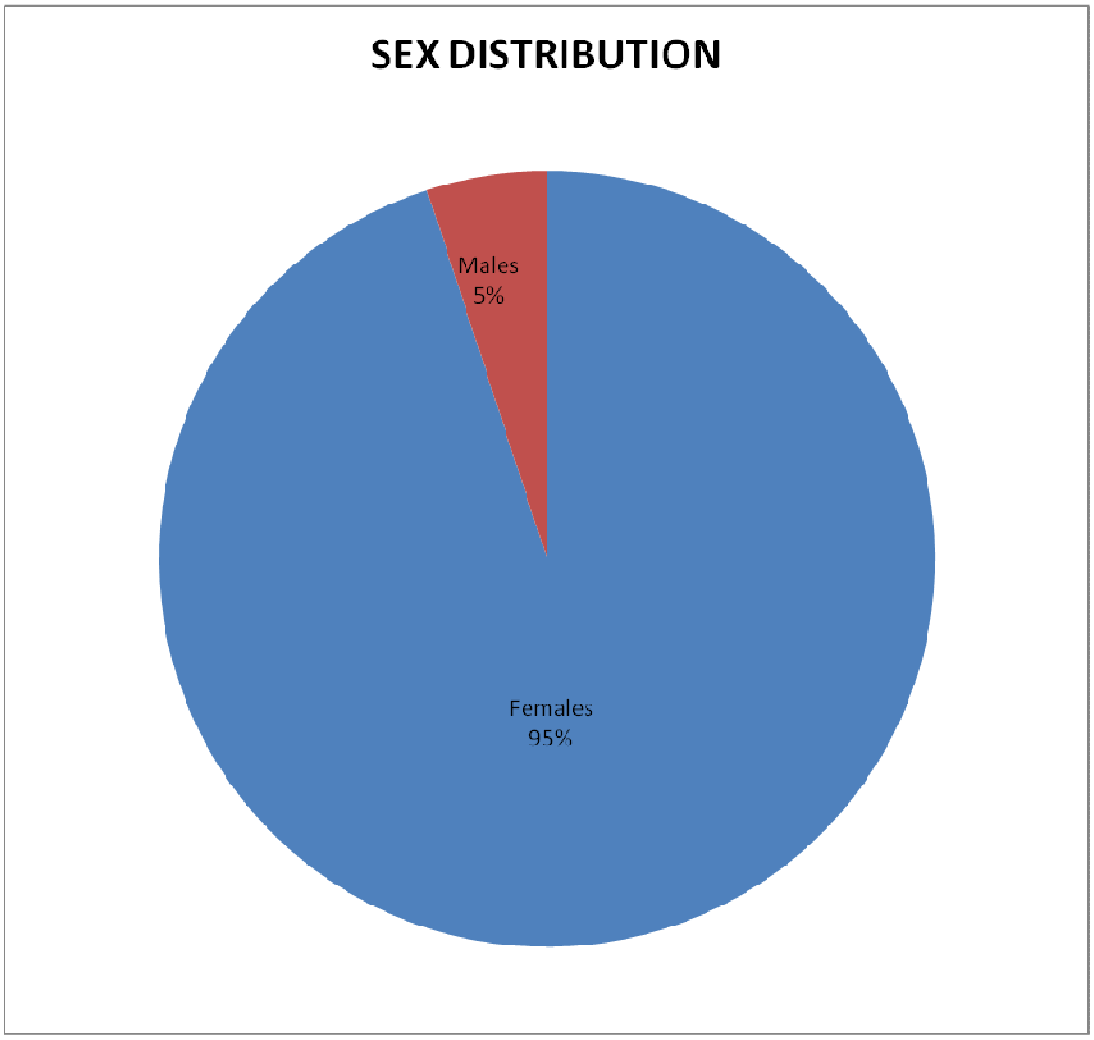
AND

RESULTS


AGE AND SEX DISTRIBUTION
MALE
FEMALE
TOTAL
0
3
3
1
20
21
0
11
11
1
3
4
0
1
1
13-20
21-30
31-40
41-50
51-60

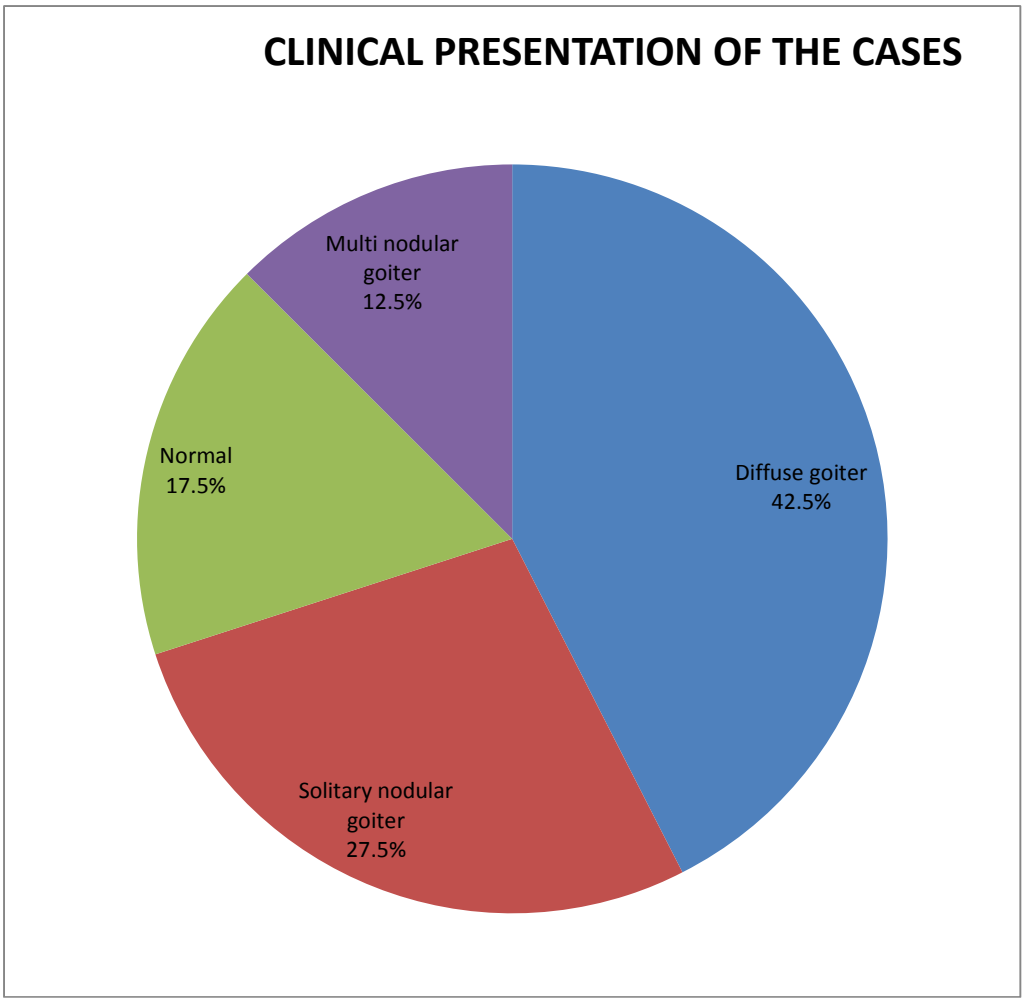
AGE AND SEX DISTRIBUTION

AGE GROUP [YEARS]	NO. OF FEMALE PATIENTS	NO. OF MALE PATIENTS	TOTAL NO. OF PATIENTS
13-20	3	0	3
21-30	20	1	21
31-40	11	0	11
41-50	3	1	4
51-60	1	0	1


SEX DISTRIBUTION
Males
5%
Females
95%

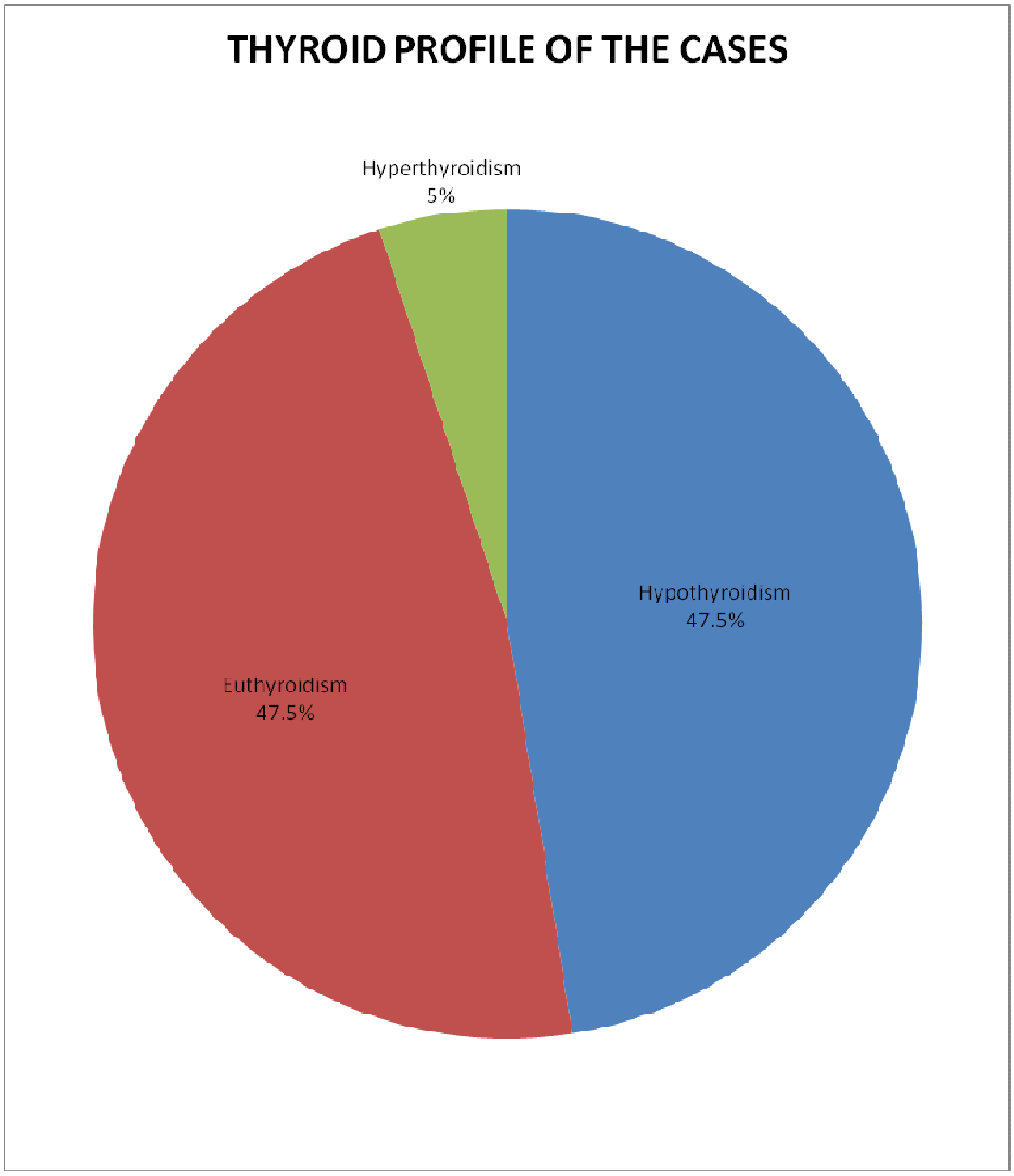
SEX DISTRIBUTION

NO. OF FEMALE PATIENTS	NO. OF MALE PATIENTS	TOTAL NO. OF PATIENTS
38	2	40

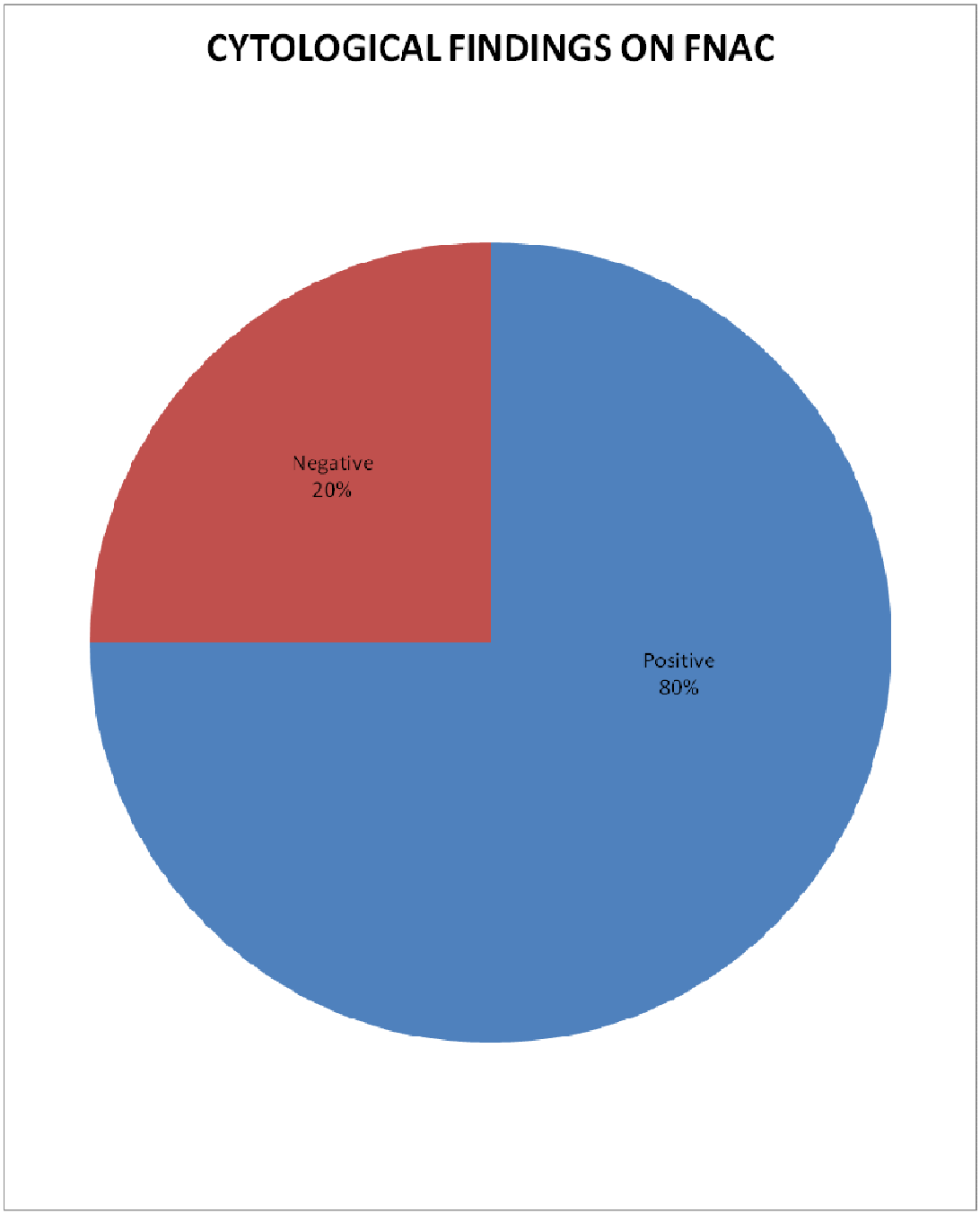

CLINICAL PRESENTATION OF THE CASES
Multi nodular goiter 12.5%
Diffuse goiter 42.5%
Normal 17.5%
Solitary nodular goiter 27.5%

CLINICAL PRESENTATION OF CASES

CLINICAL PRESENTATION	NO. OF PATIENTS
Diffuse goiter	17
Solitary nodular goiter	11
Multi nodular goiter	5
Normal	7

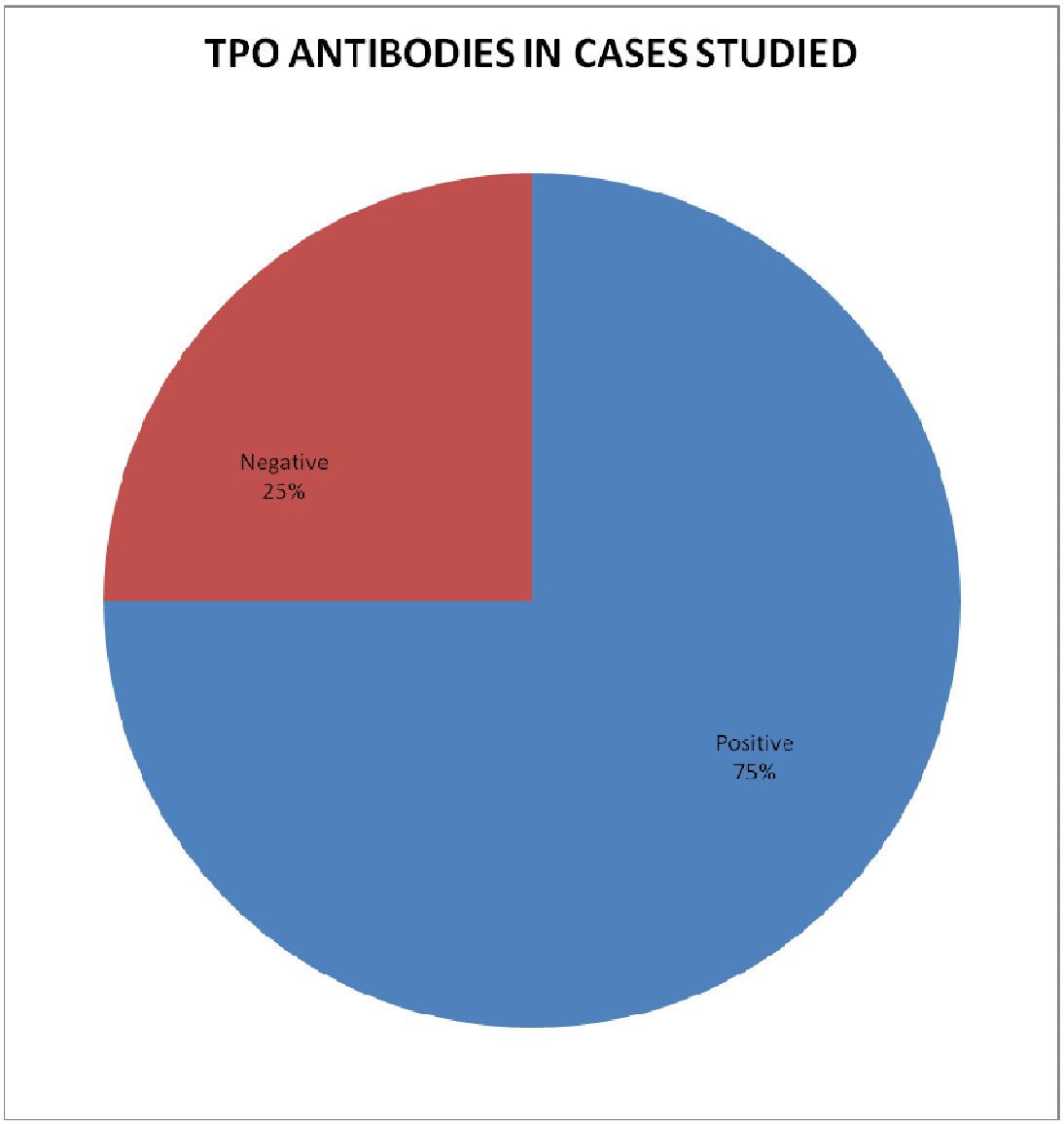

THYROID PROFILE OF THE CASES
Hyperthyroidism
5%
Hypothyroidism
47.5%
Euthyroidism
47.5%

THYROID PROFILE	NO. OF PATIENTS
Hypothyroidism	19
Euthyroidism	19
Hyperthyroidism	2


CYTOLOGICAL FINDINGS ON FNAC
Negative
20%
Positive
80%

CYTOLOGICAL FINDINGS ON FNAC

FNAC (Auto immune thyroiditis)	NO. OF PATIENTS
Positive	32
Negative	8


TPO ANTIBODIES IN CASES STUDIED
Negative
25%
Positive
75%

TPO ANTIBODIES IN CASES STUDIED

TPO ANTIBODY	NO.OF PATIENTS
Positive	30
Negative	10

CORRELATION BETWEEN CLINICAL PRESENTATION AND TPO ANTIBODY

CLINICAL PRESENTATION	TPO ANTIBODY		TOTAL
	POSITIVE	NEGATIVE	
NORMAL	7	0	7
	100.00%	0.00%	100.00%
DIFFUSE GOITER	14	3	17
	82.40%	17.60%	100.00%
SNG	9	2	11
	81.80%	18.20%	100.00%
MNG	0	5	5
	0.00%	100.00%	100.00%
TOTAL	30	10	40
	75.00%	25.00%	100.00%

P VALUE 0 .001

CLINICAL PRESENTATION AND TPO ANTIBODIES

- In our study, there is significant correlation between clinical presentation and TPO antibodies present.
- P-value=0.001
- From this report ,TPO antibodies most commonly positive in the non goiter[Normal] patients followed by diffuse goiter then solitary nodular goiter, multi nodular goiter.

CORRELATION BETWEEN CLINICAL PRESENTATION AND FNAC

CLINICAL PRESENTATION	FNAC		TOTAL
	POSITIVE	NEGATIVE	
NORMAL	7	0	7
	100.00%	0.00%	100.00%
DIFFUSE GOITER	17	0	17
	100.00%	0.00%	100.00%
SNG	3	8	11
	27.30%	72.70%	100.00%
MNG	5	0	5
	100.00%	0.00%	100.00%
TOTAL	32	8	40
	80.00%	20.00%	100.00%

P VALUE 0.001

CLINICAL PRESENTATION AND FNAC

- In our study, there is significant correlation between clinical presentation and FNAC showing auto immune thyroiditis present.
- P-value=0.001
- From this report, FNAC showing auto immune thyroiditis most commonly positive in diffuse goiter, non goiter[Normal], multi nodular goiter followed by solitary nodular goiter.

CORRELATION BETWEEN TPO ANTIBODY AND FNAC

TPO ANTIBODY	FNAC		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	22	8	30
	73.30%	26.70%	100.00%
NEGATIVE	10	0	10
	100.00%	0.00%	100.00%
TOTAL	32	8	40
	80.00%	20.00%	100.00%

P VALUE-0.068

TPO ANTIBODIES AND FNAC

- In our study shows no significant correlation between auto antibodies and cytological findings on FNAC.
- P-value=0.068
- Sarwat Fatima et al study showed significant correlation between auto antibodies and cytological findings on FNAC.

ANALYSIS AND DISCUSSION

ANALYSIS AND DISCUSSION

AGE DISTRIBUTION

- In my study results shows autoimmune thyroiditis more common in younger age group mostly between 21-30yrs.
- Similar findings observed in staii et al(2010) that study showed auto immune thyroiditis more common in younger age group(pre menopausal women)[11].
- kapila et al(1995) study showed auto immune thyroiditis more common in age group of 16-35years[12].
- Sarwat Fatima et al(2014) study showed auto immune thyroiditis more common in age group of 21-30 years.

SEX DISTRIBUTION

- In our study, auto immune thyroiditis mostly affect females.
- Staii et al(2010) study showed auto immune thyroiditis more common in females(11).
- Kapila et al(1995) study showed auto immune thyroiditis more common in females(12).
- Sarwat Fatima et al(2014) study showed auto immune thyroiditis more common in females.

Clinical presentation

- In our study , diffuse goiter is most common presentation followed by solitary nodule thyroid then multi nodular goiter.
- Kapila et al study showed auto immune thyroiditis most commonly present as a diffuse goiter followed by solitary nodule thyroid then multi nodular goiter(12).

- Sarwat Fatima et al study showed auto immune thyroiditis most commonly present as a diffuse goiter followed by solitary nodule thyroid then multi nodular goiter(20).

THYROID PROFILE

- In our study, the most common thyroid profile is hypothyroidism followed by euthyroidism then hyperthyroidism.
- Kapila et al study showed the most common presentation was euthyroidism(12)
- Sarwat fatima et al study showed the most common presentation hypothyroidism followed by euthyroidism(20)
- Esbeih A T et al(17) study showed the most common presentation euthyroidism.

CLINICAL PRESENTATION AND TPO ANTIBODIES

- In our study, there is significant correlation between clinical presentation and TPO antibodies present.
- P-value=0.001
- From this report ,TPO antibodies most commonly positive in the non goiter[Normal] patients followed by diffuse goiter then solitary nodular goiter, multi nodular goiter.

CLINICAL PRESENTATION AND FNAC

- In our study, there is significant correlation between clinical presentation and FNAC showing auto immune thyroiditis present.
- P-value=0.001
- From this report, FNAC showing auto immune thyroditis most commonly positive in diffuse goiter, non goiter[Normal],multi nodular goiter followed by solitary nodular goiter.

TPO ANTIBODIES AND FNAC

- In our study, no significant correlation between auto antibodies and cytological findings on FNAC.
- P-value=0.068
- Sarwat fatima et al study showed significant correlation between auto antibodies and cytological findings on FNAC.

CONCLUSION

CONCLUSION

- From this study ,we know auto immune thyroiditis more commonly affect younger age group.
- Auto immune thyroiditis more commonly affect females.
- Auto immune thyroiditis most commonly present as a diffuse goiter followed by solitary nodular goiter then multi nodular goiter.
- Auto immune thyroiditis most commonly present as a hypothyroidism followed by euthyroidism then hyperthyroidism.
- There is significant correlation between TPO antibodies positivity and clinical presentation. TPO antibodies most commonly positive in the non goiter[Normal] patients followed by diffuse goiter then solitary nodular goiter, multi nodular goiter.
- There is significant correlation between FNAC showing auto immune thyroiditis and clinical presentation.

- FNAC showing auto immune thyroiditis most commonly positive in diffuse goiter, non goiter[Normal], multi nodular goiter followed by solitary nodular goiter.
- There is no significant correlation between auto antibodies levels and cytological findings on FNAC.

BIBLIOGRAPHY

BIBLIOGRAPHY

[13]TA. Esbeith; *JRMS* June **20**[1] H.Hashimoto Z. Kenntniss der lymphomatösen Veränderung der Schilddrüse (Struma lymphomatosa). *Arch Klin*

Chir **1912**; 97:219-48.

[2] IM. Roitt, D. Doniach, PN. Campbell, RV. Hudson. *Lancet* **1956**; 2: 820-1.

[3] J. Slatosky, B. Shipton, H. Wahba, *Am Fam Physician* **2000**; 61: 1047-54.

[4] JI. Hamburger, *Ann Intern Med* **1986**; 104: 219-24.

[5] http:/en.wikepedia.org/wiki/Autoimmune thyroiditis.

[6] A. Costa, B. Torchio, G. Zoppetti, E. Feyless, *J Endocrinol Invest* **1989**;12:355-6.

[7] D. . Divendra, GC. Eisenberth,: *J Allergy Clin Immunol* **2003**; 111; 624-636.

[8] Goellner JR, Gharib H, Grant CS, et al. Fine needle aspiration cytology of the thyroid, **1980** to 1986. *Acta Cytol*

1987; 31:587-90.

[9] YC: Oertel. *Endocrinol Metab Clin North Am* **1996**; 25:69-91.

[10] http://www.thyroid manager .org/chapter/hashimotos thyroiditis.

[11]A. Satii, S. Mirocha, K. Todorva-Koteva, S. Glinberg, JC. , Jaume. *Thyroid Research* **2010**,3:11.

[12]K. Kapila, AS. Sathar, AN. Al-Rabah, A. Prahash, SM. Seshadri. *Annals of Saudi Medicine*, Vol 15, No 4,

1995.

04; 11(1): 67-70.

ANNEXURE

STUDY ON CLINICAL,SEROLOGICAL, CYTOLOGICAL CORRELATION IN CASES OF AUTOIMMUNE THYROIDITIS

PROFORMA

NAME: AGE: SEX: 1.M 2.F

ADDRESS: CONTACT NO:

OCCUPATION :

HISTORY

H/O Hyperactivity, irritability YES/NO

H/O Heat intolerance and sweating YES/NO

H/O Palpitations YES/NO

H/O Fatigue and weakness YES/NO

H/O Weight loss with increased appetite YES/NO

H/O Diarrhea YES/NO

H/O Oligomenorrhea, loss of libido YES/NO

H/O Dry skin YES/NO

H/O Feeling cold YES/NO

H/O Hair loss YES/NO

H/O Difficulty concentrating and poor memory YES/NO

H/O Constipation YES/NO

H/O Weight gain with poor appetite YES/NO

H/O Dyspnea YES/NO

H/O Hoarse voice YES/NO

H/O Menorrhagia YES/NO

H/O Paresthesia YES/NO

H/O Impaired hearing YES/NO

RELEVENT CLINICAL EXAMINATION

Tachycardia YES/NO

Tremor YES/NO

Goiter	YES/NO
Warm, moist skin	YES/NO
Muscle weakness, proximal myopathy	YES/NO
Lid retraction or lag	YES/NO
Gynecomastia	YES/NO
Dry coarse skin; cool peripheral extremities	YES/NO
Puffy face, hands, and feet (myxedema)	YES/NO
Diffuse alopecia	YES/NO
Bradycardia	YES/NO
Peripheral edema	YES/NO

INVESTIGATIONS

- THYROID FUNCTION TEST

  TSH

  FREE T3

  FREE T4

- TPO-ANTIBODIES

- FNAC

INFORMED CONSENT

Govt. Stanley medical college, chennai – 600001

Informed consent

Study on clinical,serological, cytological correlation in cases of autoimmune thyroiditis

Place of study: govt. Stanley medical college, Chennai

I ……. have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study.

Volunteer:

Name and address

Signature/thumb impression:

Date:

Witness:

Name and address

Signature/thumb impression

Date:

Investigator

Signature and date

அரசு.ஸ்டான்லிமருத்துவகல்லூரி, சென்னை – 600001

Study on clinical,serological, cytological correlation in cases of autoimmune thyroiditis

நான்இந்தஆராய்ச்சியில்விவரங்களைமுற்றிலும்புரிந்துகொண்டேன்.

ஆய்வில்பங்குஎடுத்துபோது,
சாத்தியமானஅபாயங்கள்மற்றும்பயன்களைபற்றிநான்அறிந்துள்ளேன்.

நான்எந்தவொருவேளையிலும்ஆய்வில்இருந்துதிரும்பமுடியும்,
அதன்பின்னர்,
நான்வழக்கம்போல்மருத்துவசிகிச்சைபெறமுடியும்என்றுபுரிந்துகொள்கிறேன்

நான்ஆய்வில்பங்குஎடுத்துபணம்எதையும்பெறமுடியாதுஎன்றுஅறிந்துள்ளேன்.

இந்தஆய்வின்முடிவுகள்எந்தமெடிக்கல்ஜர்னலில்வெளியிடப்படஇருந்தால்நான்எதிர்க்கவில்லை,
என்தனிப்பட்டஅடையாளத்தைவெளிப்படுத்தப்பட்டுஇருக்ககூடாது.

நான்இந்தஆய்வில்பங்கெடுப்பதன்மூலம்நான்என்னசெய்யபோகிறேன்என்றுதெரியும்

நான்இந்தஆய்வில்என்முழுஒத்துழைப்பையும்கொடுப்பேன்என்றுஉறுதியளிக்கிறேன்.

தன்னார்வளர் சாட்சி

பெயர்மற்றும்முகவரி
பெயர்மற்றும்முகவரி

கையொப்பம் / விரல்ரேகை: கையொப்பம் / விரல்ரேகை:

ஆராய்ச்சியாளராக
கையொப்பம்மற்றும்தேதி